Allergy Abstracts

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Asthma and Hay Fever

Prednisolone Snuff in Hay-Fever. A Controlled Trial. Godfrey, M. P., Maunsell, K., and Pearson, R. S. B.: Lancet **1**: 767, 1957.

The authors studied 46 patients (23 males and 23 females), ranging in age from 12 to 54, who were suffering from grass pollinosis. Ten of the patients also had bronchial asthma. None of these patients had received pollen therapy for at least one year prior to the study. One-half of the group was given capsules containing 1 mg. of prednisolone with 144 mg. of lactose; the other half was given capsules containing 145 mg. of lactose only. The average particle size was 20 μ. Each patient was given a nasal insufflator to apply the snuff to each nostril, the capsules being pierced at both ends and then inserted into the insufflator for use. The dose suggested was the contents of one capsule twice daily, applied in equal amount to each nostril. Antihistamine tablets were given to all subjects, and they were instructed to use them if the nasal insufflations did not provide adequate control of their symptoms. Each patient

was requested to keep a daily record of the severity of symptoms and the number of antihistamine tablets used. Records were kept from the middle of May until July 7, 1956, and this interval was divided into three periods. The two weeks beginning the middle of May were used to assess the severity of symptoms in each group; no snuff was given during this time, but antihistamine tablets were taken as required to control the patient's symptoms. The entire month of June served as a trial period during which the insufflator was given to all patients and antihistamine tablets were taken according to the individual's needs. The first week in July was a control period when antihistamine tablets alone were taken.

Only 38 of the original 46 patients completed the study. During the initial trial period it was found that the amount of symptoms experienced by each of the two groups was essentially similar, and it was assumed that these groups would be comparable for proper evaluation of the results of hormone snuff therapy. During the month of June the results suggested that the daily inhalation of 2 mg. of prednisolone snuff was of considerable help in controlling hay fever symptoms since fewer antihistamine tablets were required by the group receiving the hormone therapy. However, there was no significant difference in the number of days of hay fever experienced by the two groups during the study period. Most of the patients who used the snuff were of the opinion that the treatment was beneficial. No side effects were observed following the inhalation of prednisolone and the authors state that this form of therapy may be very beneficial in the treatment of seasonal rhinitis. R. W.

The Incidence of Allergic Disease in the General Practice of Pediatrics. Crook, W. G., Harrison, W. W., and Crawford, S. E.: J. Pediat. **52**: 20, 1958.

The allergic status of 1,225 children seen by a group of pediatricians over a period of 33 months was appraised. The patients were seen on 60 selected "study dates" and their charts were reviewed with reference to family history, type of complaint, past medical history, interval notes, physical and laboratory findings, and response to treatment. Each child was then placed in one of the following four categories: allergic, nonallergic, unknown, and probably allergic.

One hundred seventy-five of the patients (14 per cent) were classified as being allergic. They included children with infantile eczema, bronchial asthma, seasonal hay fever, allergic rhinitis (positive nasal smear for eosinophiles), and a small number of children with such disorders as intestinal allergy and allergic tension-fatigue syndrome. The 175 patients presented a total of 394 allergic complaints. Multiple allergies occurred in 77 per cent of this group. Twelve (20 per cent) of the 60 patients with eczema failed to develop any other allergic manifestation during the observation period, but 22 subsequently developed asthma. Seventy-two per cent of the eczematous children had upper respiratory allergy and/or asthma.

Of the 554 patients falling into the nonallergic group, certain ones had had occasional allergic manifestations but the "life cycle" and pattern of these children was such that these manifestations were dismissed as of a transient or minor nature.

Two hundred eighty-five children (23 per cent of the total series) were placed in the "unknown" group since their records, for one or more reasons, were inadequate or insufficient to permit more accurate classification.

There were 220 children (18 per cent) who were placed in the group labeled "probably allergic." In this group were included children with various allergic symptoms of "intermediate" degree, such as asthmatic bronchitis,

recurrent upper respiratory disease, allergic rhinitis without positive nasal smears for eosinophiles, and also those children under 2 years of age with apparent asthma. This latter group was so classified because of the difficulty in accurately differentiating the presenting symptoms from such conditions as bronchiolitis and asthmatic bronchitis at such an early age. H. F.

Outpatient Bronchodilator Therapy. Gandevia, B., Hume, K. M., and Prime, F. J.: Lancet **1**: 956, 1957.

The authors carried out a double-blind test evaluation of 4 bronchodilator drugs on 18 patients who had chronic wheezing respirations. The drugs tested were Theodrox, aminophylline suppositories, choline theophyllinate, and isoprenaline. For purposes of control, phenobarbital and a placebo containing calcium carbonate with a trace of quinine sulfate were also included in the trial study. The method of procedure was to have each patient rotate on each one of the medications for one week during a six-week period. Six groups of patients were each allotted a different drug or placebo weekly according to a preset plan.

The 18 patients whose ages ranged from 25 to 65 years were suffering from asthma, chronic bronchitis, asthmatic bronchitis, bronchitis, and emphysema. Their clinical status was evaluated by the extent of their forced vital capacity expelled in the first second (F.E.V. 1.0). Although the normal range is 75 to 80 per cent of the total forced vital capacity in the first second, the average for the patients in this study was only 51 per cent. The weekly forced expiratory volume at one second of the patients regularly assessed during the experimental period ranged only from 1,210 to 1,290 c.cm. so that the lack of variance with time made the statistical evaluation of the results from the medication more reliable.

No serious side effects were observed while the patients were taking these medications. Aminophylline suppositories and choline theophyllinate appeared to be most effective as bronchodilators, while sublingual isoprenaline was quite inconsistent and Theodrox produced only a minimal change in the patient's forced expiratory volume at one second. Although many patients felt that the placebo and several of the test drugs did not suit their particular needs, none had an unfavorable response to phenobarbital and 9 of the 15 patients who completed the study felt that the phenobarbital was quite beneficial.

The authors conclude that the most satisfactory form of outpatient therapy for wheezing dyspnea would be a combination of phenobarbital with one of the effective bronchodilators. R. W.

Asthmatic Wheezing. Compression of the Trachea and Major Bronchi as a Cause. Dekker, E., and Groen, J.: Lancet **1**: 1064, 1957.

The authors studied the mechanism of wheezing in asthmatic patients with special emphasis on the importance of narrowing of the trachea and larger bronchi in producing this symptom. A series of healthy persons and asthmatics were taught how to wheeze. Frontal, transverse, and oblique x-ray exposures were made of the dynamic changes which occurred in the diameter of the trachea and large bronchi of the normal subjects and asthmatics during inspiration and voluntary wheezing expiration. The same type of studies were made on asthmatic patients during spontaneous attacks. Artificially induced wheezing in a normal subject narrowed the lumen of the trachea as far down as the lower part of the cervical portion. A similar narrowing of

the main airways was also seen during voluntary wheezing expirations in patients with asthma and emphysema. The narrowing observed in the tracheobronchial tree of the asthmatic and emphysematous patient was strikingly similar to the findings observed in normal subjects during severe spontaneous attacks of wheezing. When human lungs removed at autopsy were made to "breathe" under varying positive pressures in a closed jar, it was found that an expiratory pressure of 1 cm. of mercury or more produced a considerable narrowing by prolapse of the membranaceous portion of the trachea and bronchi into the lumen of the air passages. The authors state that passive compression of the larger air passages in the asthmatic patient by high intrathoracic expiratory pressure produces a narrowing of the main airways and is an important factor in the causation of asthmatic wheezing. It is suggested that proper breathing exercises might be most beneficial in helping to alleviate the mechanism responsible for the wheezing. R. W.

Antigenic Analysis by Gel Diffusion. III. Pollens of the Amaranth-Chenopod Group. Wodehouse, R. P.: Ann. Allergy **15**: 527, 1957.

The Ouchterlony double diffusion gel technique was employed to study the antigenic patterns of the pollen extracts of four common hay fever-producing members of the *Amaranthaceae* family and of five common hay fever plants of the *Chenopodiaceae* family. The antigenic pattern of each of these pollens was compared with each member of its own family and with those of the other group. Anticarelessweed rabbit serum was used for studying the *Amaranthaceae,* and Russian thistle rabbit antiserum was the antibody employed for the studies of the *Chenopodiaceae.* All members of the *Amaranthaceae* were found to contain the same antigens in nearly the same proportion. The *Chenopodiaceae,* on the other hand, varied considerably in their antigenic components. None of the members of this group, except burning bush and Russian thistle, had similar precipitation patterns. These two extracts possessed 4 common antigen bands, which appeared also to be common to the members of the *Amaranthaceae.* The lack of antigenic similarity among the *Chenopodiaceae* pointed to the necessity of individualized therapy for patients sensitive to the members of this plant family, whereas patients sensitive to the *Amaranthaceae* can be adequately treated with an extract of any one member of this group. H. F.

Xiphodynia as a Concomitant of Asthma. Malloy, C. J.: Canad. M. A. J. **77**: 585, 1957.

Two asthmatic patients who complained of pain over the xiphoid process and cartilage were studied. The first patient was a 55-year-old obese woman who had myocardial insufficiency, psychoneurosis, and intermittent attacks of bronchial asthma. Pressure over the xiphoid caused pain and occasionally would initiate asthma. Adrenaline relieved the dyspnea but not the xiphoid pain. The application of ethyl chloride spray or the injection of procaine into the tissues adjoining the xiphoid sternal junction temporarily abolished her pain but did not prevent its recurrence. The second patient was a 47-year-old man with a four-year history of asthma. His medical work-up failed to disclose any organic pathology. This patient also obtained temporary relief of his pain following the application of ethyl chloride spray or the injection of procaine. Neither patient noticed any association between the frequency and severity of asthma and the degree of tenderness and pain over the xiphoid process. Each experienced a gradual regression of the pain and tenderness after a matter of many months. The author states that xiphodynia may occur as a concomitant symptom of bronchial asthma but that there does not appear to be any relationship between the two. R. W.

Dermatology

Contact Dermatitis From Algerian Ivy. Dorsey, C. S.: Arch. Dermat. **75**: 671, 1957.

The author described two cases of contact dermatitis resulting from exposure to Algerian ivy. The first patient was a 34-year-old male physician who developed a pruritic urticariopapular rash over the extensor surfaces of both knees and the dorsa of both hands and wrists. On six successive week ends he had been uprooting a patch of Algerian ivy. The patient showed a strongly positive patch-test reaction to crushed leaves and stems of this plant.

The second patient was a 76-year-old retired minister with an urticariovesicular dermatitis in streaks and plaques over the extensor surfaces of the forearms, upper chest, and face. He suggested that a broad-leaved ivy might be the cause, as he had trimmed the plants a few days previously. The rash gradually cleared, but the patient developed another eruption after brushing his face against the cut stem of the same broad-leaved ivy. The leaves of the plant were subsequently identified as *Hedera canariensis* (Algerian ivy). Several months later this patient was patch-tested with English ivy and got a positive reaction.

When 6 normal persons were patch-tested with the juice of Algerian ivy, 5 had negative reactions and one developed a mild urticarial response which persisted for a week. This patient had trimmed Algerian ivy on a fence two weeks previously, but had experienced no dermatitis following this exposure. Although the control series was small, the author states that the findings rule out the possibility that Algerian ivy is a primary irritant. In conclusion, the author suggests that less common types of ivy probably are a more frequent cause of contact dermatitis than is generally suspected. R. W.

Idiosyncrasy to One Tablet of Meprobamate. Davis, E.: Harefuah **53**: 37, 1957.

Two cases of untoward reactions to Meprobamate are reported. The first patient, a 36-year-old man, took one 400 mg. tablet of Meprobamate and 4 hours later developed chills and intense itching over the pelvic region. The next day he had a purpuric rash, with single and confluent lesions extending from the umbilicus to the upper thighs. The rash cleared within four days. The bleeding time, clotting time, and the number and form of thrombocytes were normal. The patient had had minor allergic reactions to drugs in the past.

The second patient was a 41-year-old woman who developed intense itching of the pelvic region and nipples, pain in the breasts and axillae, and malaise 5 hours after taking one tablet of Meprobamate. On the next day a well-demarcated erythema appeared on the pelvic region, axillae, and breasts. The lesions disappeared in a few days. The patient gave a past history of allergy to penicillin. I. G.

Chromate Dermatitis. Its Natural History and Treatment. Bernhardt, H. J.: Arch. Dermat. **76**: 13, 1957.

Chromate dermatitis occurred frequently among workers employed in an aircraft factory. Positive patch test reactions to 0.5 per cent solution of potassium dichromate were obtained. Exposure to chromate can occur by the inhalation of chromate dust from distant sections of the factory. Chromate dermatitis tends to heal slowly. Even when all contact with the excitant is avoided, complete healing may not take place for about 12 weeks. Chromate

dermatitis often simulates nummular eczema and may produce chronic eczema or neurodermatitis. In many patients other sensitivities develop to complicate treatment and prolong the illness.

Some of the patients in the series were on strike for a period of three months. The healing process was slow, even though these patients were no longer being exposed to chromate. During this period, routine dermatologic preparations consisting of boric acid compresses, bland lotions, zinc oxide paste, and mild tars were ineffective. Both 1 per cent hydrocortisone ointment plus neomycin and 0.5 per cent prednisolone plus neomycin were highly effective at this time but much less so while the patient was exposed to chromate. Prednisolone 0.5 per cent with neomycin seemed to be superior to hydrocortisone 1 per cent with neomycin in producing a rapid response to treatment and in reducing the relapse rate. R. W.

The Role of Allergic Phenomena in the Etiology and Pathogenesis of Atopic Dermatitis. Milder, E.: Arch. Dermat. **76**: 27, 1957.

A study of 84 patients with atopic dermatitis is reported. Scratch tests were performed with milk and egg extracts on 53 youngsters under 16 years of age who had atopic dermatitis and on a control group of 30 nonatopic children. Among the allergic patients there were 62 per cent positive reactions, as compared to 30 per cent positive reactions among the normal controls.

Five children, varying in age from 4 to 9 years, who had numerous positive reactions to foods and inhalants were hospitalized. They immediately began to improve without special therapy or diets. When they returned home their skin conditions quickly grew worse. When they were sent to stay with relatives who lived in a similar environment, they again improved as quickly as they had previously in the hospital. Another group of 6 patients, from 17 to 21 years of age, spent 6 or 7 weeks in an area 3,000 feet above sea level. Although they wore more woolen underclothing, their condition improved rapidly.

The population from which the patients were selected was 80 per cent agricultural and 20 per cent industrial. The incidence of atopic dermatitis was found to be higher among patients from an industrial environment.

The author reports that the positive skin test reactions in his patients did not appear to be related to the clinical course of the disease. He concludes that allergic sensitivity is of little etiological importance in atopic dermatitis, although allergic factors may occasionally produce exacerbations in some patients. Factors other than allergy are more likely to precipitate the condition. R. W.

Topically Applied Prednisone and Prednisolone in the Treatment of Selected Dermatoses. Frolow, G. R., Witten, V. H., and Sulzberger, M. B.: Arch. Dermat. **76**: 185, 1957.

The comparative effectiveness of 0.5 per cent prednisone, 0.5 per cent prednisolone, and 1 per cent hydrocortisone was studied in a series of private patients with various skin diseases. The medicaments were incorporated into the same vehicle and the vehicle alone was used as a control. There was no essential difference between the effectiveness of topically applied prednisone and prednisolone. Neither the prednisone nor the prednisolone in 0.5 per cent concentration of the original batch of ointments was as effective as the hydrocortisone in 1 per cent concentration, but later batches appeared to be as effective as the hydrocortisone ointment. It was noted, however, that 4

cases using the original 0.5 per cent prednisone and prednisolone became worse both objectively and subjectively, while under treatment with these products. They subsequently showed improvement when treated with 1 per cent hydrocortisone. R. W.

Osmylogenic Urticaria. Derbes, V. J., and Krafchuk, J. D.: Arch. Dermat. **76**: 103, 1957.

Three cases of urticaria apparently due to inhalation of odoriferous substances are reported. The first patient was a 42-year-old woman with ragweed hay fever who developed urticaria repeatedly during the ragweed season with rapid remission after the pollen season. Her urticaria was subsequently controlled by pollen therapy. The second case observed was an 11-year-old boy with ragweed asthma, who would develop asthma and urticaria following exposure to paint fumes during each ragweed season. Although the asthma would clear rather quickly, the urticaria persisted for three or four days. He failed to react to a skin test with linseed oil, but he had a positive reaction to cottonseed, an antigen closely related to linseed. The third patient was a 9-year-old youngster with asthma since infancy, who had a marked sensitivity to fish. This child developed generalized hives and angioneurotic edema whenever certain types of fish were fried in the home.

The authors stress the fact that urticaria can occur from the inhalation of air-borne materials by absorption through the conjunctiva or respiratory tract. R. W.

Miscellaneous Allergies

Penicillin Anaphylaxis. A Case Report and Some Notes on Its Prevention. Keohane, J.: Canad. M. A. J. **77**: 695, 1957.

The author reports a case of acute, fatal anaphylaxis following a penicillin injection in a 20-year-old man. Twenty-four hours following a submucous resection, the patient developed a slight elevation in temperature and was given a routine injection of 800,000 units of Duracillin as a precautionary measure. Two hours following the injection he suddenly went into severe shock without loss of consciousness. Although there was no apparent respiratory obstruction, he was bluish-gray in color and his blood pressure and pulse were imperceptible. Heart sounds were barely audible and his reflexes appeared normal. He was given continuous oxygen by mask, Vasoxl intravenously, coramine intravenously, and an intravenous drip containing l-norepinephrine in 5 per cent dextrose. Twenty units of ACTH and 100 mg. of hydrocortisone were added to the drip. A second drip of 500 c.c. of dextran was also started and approximately one hour later he was somewhat improved, his blood pressure having risen to 60 and his pulse rate to 140. He was given two 0.5 c.c. injections of Adrenaline later in the day and his condition remained static except for some intermittent bouts of vomiting and hiccups.

During the next 24 hours, he received 10 c.c. of Levophed in 2,000 c.c. of 5 per cent dextrose intravenously, 500 c.c. of dextran, and 1,500 c.c. of plasma. He appeared much improved and his color was good, even though he was no longer receiving oxygen. His blood pressure was 100/70 and his pulse was 100. His temperature was normal, whereas the previous afternoon it had been 103° F. Since the patient's condition was somewhat puzzling and it was not certain whether his acute reaction was caused by penicillin allergy or an acute overwhelming infection, it was decided to place him on antibiotic

therapy. He was given 1 gram of chloramphenicol intramuscularly, 25 mg. of cortisone orally every 4 hours, and 50 mg. of Phenergan intramuscularly twice daily. Because of his frequent vomiting, he was continued on 3,000 c.c. of intravenous fluids that day. The next morning, approximately 42 hours after the onset of the acute reaction, he became cyanosed, his pulse rate rose rapidly, and his blood pressure was unobtainable. He showed signs of acute pulmonary edema and circulatory collapse, vomited several times, became restless, went into coma, and died approximately one hour later.

At autopsy all the organs except the lungs were normal. The bronchi were full of blood-stained frothy liquid and the alveoli were filled with fluid. Anatomically, the picture was that of acute pulmonary edema. His past history revealed that he had had some topical penicillin 8 years previously for relief of impetigo but he had never received penicillin parenterally. He had had urticaria of unknown etiology 9 years previously and eczema as an infant. The author strongly discourages the use of penicillin topically because of its strong sensitizing properties. He further emphasizes that penicillin should not be given to any patient with a proven history of allergic disease because of the serious consequences that may occur from penicillin reactions in such individuals. R. W.

Severe Sensitivity Reaction (Hepatitis, Dermatitis and Pyrexia) Attributable to Phenylindanedione. East, E. N., and Beamish, R. E.: Canad. M. A. J. **77**: 1028, 1957.

A 64-year-old man with a three-day history of recurrent angina and ECG evidence suggestive of coronary disease was given heparin (50 mg.) intravenously every 4 hours for 24 hours and then started on phenylindanedione (50 mg.) in divided doses. On his fifteenth hospital day the patient developed a diffuse, itchy, erythematous macular eruption on the back and upper abdomen which soon became generalized and involved the face and extremities. The pruritus failed to respond to local applications or to antihistamines and continued unabated for the next 3 days. At first it was thought that the rash might have been caused by a dermatitis medicamentosa from barbiturates, but even after this medication was discontinued the rash persisted. Twelve days after the onset of the rash the patient developed a fever for the first time, and three days later he became jaundiced. The liver was palpable below the costal margin, the icteric index was 15 units, the alkaline phosphatase was markedly elevated and there was a positive cephalin flocculation test and thymol turbidity test. The sedimentation rate continued to be markedly elevated and the white blood count was slightly elevated. Thirteen days after the onset of the rash PID was discontinued and Tromexan was substituted as an anticoagulant for the next five days, when it too was discontinued. The prothrombin time gradually returned to normal but the anorexia, rash, and fever persisted for another 6 days, although the patient did not appear seriously ill. He was given Meticorten orally, with improvement; one week later the rash had cleared completely and the liver margin was only barely palpable. Soon after he was given Meticorten his temperature quickly returned to normal. The Meticorten had to be continued for three weeks because of persistent pruritus which recurred when the dosage was reduced. Since all other possible causes for the patient's clinical reaction were eliminated, the author concluded that this patient had a severe allergic reaction to phenylindanedione. The fact that all his remaining symptoms regressed so rapidly when steroid therapy had been started further tends to substantiate the likelihood that an allergic reaction was responsible for the acute symptom complex. R. W.

Fatal Agranulocytosis During Carbimazole Therapy. Tait, G. B.: Lancet **1**: 303, 1957.

A 66-year-old man developed a fatal agranulocytic reaction while receiving carbimazole therapy. The patient had mild congestive failure, auricular fibrillation, and a definite enlargement of his thyroid gland. A diagnosis of left ventricular failure with atrial fibrillation due to hyperthyroidism from a nodular goiter was made. The blood count was normal. The patient was started on chlortetracycline and digoxin. He was also given a test dose of 0.5 ml. of intramuscular mersalyl, after which he collapsed and developed an alarmingly rapid pulse rate. He made an uneventful recovery and was given no further mercurial diuretic therapy. He was simultaneously started on carbimazole, 10 mg. three times daily. A few weeks later, he was given Furadantin because of a persistent *Staphylococcus aureus* urinary tract infection. His white cell counts during this time ranged from 7,000 to 21,000 per c.mm. with a high percentage of neutrophila. During the eleventh week of carbimazole therapy, he suddenly developed a high temperature and became acutely ill. The white cell count showed just 300 white blood cells, of which only 6 per cent were neutrophils. The hemoglobin was 62 per cent. Treatment with penicillin and blood transfusions was instituted immediately, but the patient deteriorated rapidly and died within three days. Post-mortem examination revealed an enlarged prostate, cystitis, and a nodular goiter. The heart was considerably enlarged. The author believes that this patient had a fatal agranulocytosis from carbimazole therapy. He also had observed two other patients who developed a neutropenia while receiving this medication. In these cases, the neutropenia cleared spontaneously when the drug was stopped. The importance of frequent blood counts is stressed as a possible aid in the prevention of serious agranulocytic reactions from carbimazole. R. W.

Apparent Sensitization to Novobiocin: Case Report. Hughes, J. G.: J. Pediat. **51**: 664, 1957.

A 7-month-old infant was treated with 125 mg. of novobiocin (Albamycin) orally 3 times daily for 4 days. Three days following the discontinuance of the medication he became very irritable and developed a fever which was followed in 2 days by the appearance of a macular rash about the skin of the extremities. Rubella was at first suspected but was ruled out when on the same day the child developed a raw, red, spreading lesion about the lips and severe inflammation of the mucosa of the mouth and tongue along with an extension of the erythematous skin rash which involved most of the body. The infant also began to develop severe edema of the hands, feet, fingers, and toes, along with marked pain in these areas. This was interpreted as being due to allergic involvement of the small joints. The child was hospitalized, given symptomatic therapy and intramuscular injections of hydrocortisone, and made a rapid recovery. H. F.

Anaphylaxis

Comparative Inhibition of Anaphylaxis in Mice by Steroids, Tranquilizers, and Other Drugs. Fox, C. L., Jr., Einbinder, J. M., and Nelson, C. T.: Am. J. Physiol. **192**: 241, 1958.

Some of the steroids and various other drugs possessing specific pharmacologic properties were studied for their ability to inhibit anaphylaxis in mice. The animals were sensitized by the intraperitoneal injection of large doses of

horse serum and were then injected intramuscularly with the steroids and intraperitoneally with the other drugs 3 to 72 hours prior to the administration of a challenging dose of horse serum. Adrenolytic, hypertensive, and vasoconstrictive drugs, together with tranquilizers, antihistamines, diuretics, and anti-inflammatory agents, were tested. The degree of protection provided by the medications was determined by a comparison of the survival rate of treated sensitized mice with the incidence of fatal anaphylaxis in untreated sensitized animals. Chlorpromazine, promazine, reserpine, lysergic acid diethylamide, prednisolone, prednisone, fluorohydrocortisone, and cortisone all gave excellent protection for periods varying from 5 to 48 hours. Meprobamate, sedatives, antihistamines, anti-inflammatory agents, diuretics, and such steroids as 2 dimethyl-hydrocortone and desoxycorticosterone acetate (DCA) afforded no protection. The vasoactive agents, including epinephrine, also failed to provide protection. There appears to be some correlation between the chemical structure of the steroids and their ability to protect the sensitized animal. The degree of protection afforded by the steroids was inversely proportional to the degree of sensitivity achieved in the injected mice. As the degree of sensitization increased, larger doses of drugs were required for protection. When the fatality rate in unprotected animals approached 100 per cent, few of the animals were protected by the drugs. In contrast to this, some tranquilizing drugs provided a high degree of protection at levels of maximum sensitization. Sensitized guinea pigs were protected against anaphylaxis by certain tranquilizers but not by the ones that afforded protection to mice. This is probably due to different pharmacologic properties possessed by the latter drugs and to the variation in the type of noxious agents released in the anaphylactic reactions in the two species. H. F.

Pharmacology, Physiology, and Pathology

The Steroid Feedback Mechanism. Schapiro, S., Marmorston, J., and Sobel, H.: Am. J. Physiol. **192**: 58, 1958.

A corticotropin-releasing factor (CRF) is known to originate from areas in the hypothalamus. The chemical nature of this material has not yet been determined, but it is believed to be lipoprotein in nature, or possibly pitressin or a contaminant of pitressin. High blood levels of adrenal cortical hormones act to inhibit the secretions of ACTH. This inhibitory influence was originally believed to occur at the pituitary level. The present study serves to support previous findings that the hypothalamus may also be the site of steroid inhibition. The 4-hour change in circulating eosinophils was used as the measure of ACTH secretion. Desoxycorticosterone (DCA) was the steroid employed for blocking ACTH release, since it does not affect the eosinophilic response but will prevent the release of ACTH in response to stress. When venous brain blood from a stressed hypophysectomized rat was injected into DCA-treated intact rats, a discharge of ACTH occurured in the recipients as indicated by a pronounced 4-hour eosinopenia. When carotid artery blood from stressed hypophysectomized rats was injected into intact DCA-treated animals, no change in the eosinophil count occurred, indicating a lack of ACTH secretion. When DCA was administered to the hypophysectomized donor rat, its brain blood contained little or no pituitary-stimulating activity. "It is concluded that at least one mechanism whereby high levels of the adrenal cortical hormones inhibit the release of ACTH following stress is by blocking the secretions from a cerebral structure, presumably the hypothalamus, of a pituitary stimulating substance." H. F.

Bronchospirometric Studies Relating to a Radiographic Method for Determining Differential Vital Capacity. Autio, V.: Acta med. scandinav. **158**: 329, 1957.

This monograph of approximately 100 pages describes bronchospirometry in its application to normal persons and to those having tuberculosis. A method is presented whereby it is possible to obtain maximal volume changes in the lungs by measuring the areas of lung fields on x-ray. A planimeter is used on films taken at extreme inspiration and at extreme expiration. The contribution of each lung to total volume changes is then calculated and the results are compared with those obtained on bronchospirometry. The ratio of the differences between the maximal inspiratory and expiratory areas for each lung can be taken as an approximate measure of the ratio of the volume changes (vital capacities) of the lungs. Conversion factors are presented. Good correlation was obtained between the two measures of vital capacity in a group of 67 patients having unilateral parenchymal disease, in 44 patients having parenchymal and pleural changes in only one lung, and in 25 patients with bilateral parenchymal disease. In 12 patients who had been subjected to thoracoplasty, in 23 with intrapleural pneumothorax, and in 19 with extrapleural pneumothorax, the correlation between radioplanimetry and bronchospirometry was poor. Such cases must be evaluated by bronchospirometry. With the above technique it may be possible to spare many patients the need for bronchospirometry. E. K.

Immunology

Auto-Antibodies in Addison's Disease. Anderson, J. R., Goudie, R. B., Gray, K. G., and Timbury, G. C.: Lancet **1**: 1123, 1957.

It has been demonstrated that the serum of most cases of Hashimoto's disease contains complement-fixing antibodies reacting with thyroid extract. The present study deals with sera of patients with Addison's disease to see if they show the presence of a similar type of immune antibody. Extracts of human liver, kidney, brain, thyroid, and adrenal tissues were prepared from autopsy specimens obtained within three hours of death and from thyroid and adrenal tissues removed surgically. Sections of the various organs were frozen, finely sliced, and extracted with saline solution in a mechanical shaker. The extracts were centrifuged to remove suspended tissue fragments and lipoid material and then diluted when necessary to reduce anticomplementary activity. The complement-fixation technique employed for the antibody tests is described in detail.

Antibody tests were carried out on the sera of 10 patients with Addison's disease, of 18 patients with Hashimoto's disease, of 13 patients with thyrotoxicosis, of 12 patients with Simmond's disease, and of 55 patients in a general medical-surgical ward who were known not to have any specific endocrine disturbance. Two of the ten cases of Addison's disease had evidence of tuberculosis. Several specimens of each tissue extract were tested and the amount of complement fixation varied with different thyroid and adrenal extracts. In two cases of Addison's disease titers of the sera examined for complete inhibition of lysis varied between 0 and 16 with different adrenal extracts. Even with the weakest-reacting extracts, however, partial inhibition of lysis was observed, whereas all the other sera were completely negative when tested with all the adrenal extracts. Patients with Hashimoto's disease or thyrotoxicosis failed to react with adrenal extracts. The authors suggest that an antiadrenal antibody may be responsible for progressive destruction of the adrenal cortex in idiopathic Addison's disease. They further

postulate that some patients with Addison's disease are likely to form both adrenal and thyroid auto-antibodies. The thyroid antibody would account for the histologic changes often seen in the thyroid gland and might explain the coexistence in one of their patients of both Addison's disease and Hashimoto's disease. The failure to find antiadrenal antibody in most of the patients with Addison's disease might be explained by the fact that adrenal cortical destruction is accompanied by disappearance of the anti-adrenal antibody. R. W.

The Significance of Blood Group Conflicts and Aberrant Salivary Secretion in Spontaneous Abortion. McNeil, C., Trentelman, E. F., Fullmer, C. D., Kreutzer, V. O., and Orlob, R. B.: Am. J. Clin. Path. **28**: 469, 1957.

Blood group and salivary secretions were studied in a group of parents who had produced 2 or more spontaneous abortive pregnancies during the first 20 weeks of gestation and in a group of parents of 3 or more children children produced without the occurrence of abortions. Blood specimens were typed for A_1, A_2, B, and Rh_o antigens and the mother's serum was crossmatched to the father's red blood cells. Saliva was tested for the presence of A, B, or H factors. Secretors in any titration above 1:4 were placed in one group; nonsecretors formed a second group. Persons of group A or B who secreted only one factor were designated as aberrant secretors. Where blood from the father and mother was incompatible, maternal blood serum was tested for antibodies to the paternal factors.

Twenty-one of 23 nonaborter couples were ABO compatible and were compatible in their ability to secrete AB and H factors in saliva. There were no aberrant secretors in this group. However, 34 of 47 couples in the aborter group were ABO incompatible or showed aberrant secretions of saliva factors. Women in the aborter group were likely either to be weak secretors of H, A, or B factors or to be nonsecretors.

A modification of genotypes is suggested to explain the new findings presented. E. K.

The Antibody (Hemagglutinin) Response as a Tool for Etiologic Diagnosis of Diarrheal Disease. Family Outbreak Associated With Paracolobactrum (Escherichia coli 075). Neter, E., and Suskind, L.: J. Pediat. **52**: 38, 1958.

Three children and one adult in a family of nine developed acute diarrheal disease. The usual pathogens, such as shigellae, salmonellae, and enteropathogenic *Escherichia coli* could not be found in stool cultures. A nonlactose-fermenting, gram-negative, coliform bacillus was isolated, however. High hemagglutinin titers to this strain were found in the sera of all four patients. There was no increase in the agglutinin titers to heterologous enteric bacteria. These findings suggest that the strain of paracolobactrum (*Esch. coli* 075) was of etiologic importance in the diarrheal disease of these patients and that the antibody response of patients may be helpful as a means of determining the etiologic role of bacteria in diarrheal diseases, particularly if combined with bacteriologic and epidemiologic data. H. F.

The Antigenic Role of the Excretions and Secretions of Trichinella Spiralis in the Production of Immunity in Mice. Campbell, C. H.: J. Parasitol. **41**: 483, 1955.

Trichinella spiralis larvae isolated from infected mice were washed and placed in a nutrient fluid in which they remained viable (motile and growing)

for 6 or 7 days. The larvae were then centrifuged from the solution and the supernate was used to immunize mice. Nutrient fluid which had not been infested with larvae was used for injection of control mice. The mice were challenged with *T. spiralis* and analyzed for degree of protection. It was found that the secretions and excretions of *T. spiralis* stimulated an immune response "as evidenced by a more rapid loss of adult worms, stunting of adult female worms, and smaller numbers of larvae recovered from injected mice as compared with control mice." E. K.

Miscellaneous

An Ester of Prednisolone Particularly Active by Local Administration. Desaulles, P. A., and Meier, R.: Schweiz. med. Wchnschr. **87**: 269, 1957.

The anti-inflammatory activity of different steroids was measured by the granuloma test. Rats were implanted subcutaneously with sterile cotton; this produced a local reaction of the mesenchyma in the form of a granuloma which could be weighed. The inhibition of this reaction by prednisolone trimethylacetate (Ultracortessol, Ciba) when administered locally (impregnated on the cotton) was far superior to the effects of cortisone acetate, hydrocortisone acetate, 9γ-fluoro-hydrocortisone, prednisone, and prednisolone in equal doses. Local and systemic administration of prednisolone trimethylacetate produced less general manifestations than the other steroids in comparable doses. I. G.

Side Effects and Complications of Vaccination Against Poliomyelitis. Baumann, T., and Felder, J.: Schweiz. med. Wchnschr. **87**: 964, 1957.

An analysis was made of the nature of the reactions which occurred after a total of 138,528 first and second doses of poliomyelitis vaccine had been given over a 4-month period. Local reactions at the injection site occurred in about 15 per cent of the group. Fever developed in 29 patients within 24 hours after the injection. Urticaria and other types of rashes were observed in 24 patients; asthma occurred in 3 cases; and polyarthritic symptoms were noted in 2. "Transient serogenetic flaccid paralysis" was reported in 8, and meningoencephalitic complications were noted in 7 patients. All of these reactions were usually of brief duration, subsiding within a few hours or days following the vaccination. M. C.

Cardiac Involvement in Anaphylactoid Purpura. MacGregor, G. A., and Vallance-Owen, J.: Lancet **2**: 572, 1957.

Three patients with purpura developed concomitant cardiac lesions which were diagnosed by electrocardiographic studies or confirmed by post-mortem findings. The first patient was a 72-year-old housewife who had intermittent abdominal pain, hematuria, hematemesis, and a symmetrical purpuric rash on the buttocks and thighs as well as a papular eruption on her elbows. The rash had been present for two years, occurred sporadically, and did not always coincide with the attacks of colic. Hematologic findings were entirely normal. There was no diminution of the platelet count, and blood chemistry studies were essentially normal. Serial electrocardiographic studies suggested the presence of either a healed anteroseptal infarct or biventricular hypertrophy. Sporadic attacks of atrial fibrillation and widespread ST changes which eventually reverted to normal were also present. There was a history of substernal pain after laparotomy during the first attack of colic. Electrocardiograms were not obtained during this incident, but cardiac infarction

probably occurred. During a recurrence two years later there was evidence of temporary myocardial damage, coinciding with the renal and intestinal involvement. The cardiac and renal signs resolved spontaneously and no causative factor for the purpura was ever elicited.

The second patient was a 53-year-old man who had a myocardial infarct in 1952. In 1956, he developed muscle pains, a productive cough, and hemoptysis. Shortly thereafter he became extremely short of breath and developed a rash on his extremities. Blood chemistrry studies were all normal and there was no diminution in his platelet count. The tourniquet test remained positive for eight weeks and he was found to have active tuberculosis. ECG studies taken after the onset of the purpura showed elevated ST segments in leads II, III, and VF and deep inversion of the T waves in all the chest leads. All these changes gradually disappeared during the ensuing eight weeks as the purpura subsided.

The third patient was a 77-year-old man who was admitted to the hospital with infected varicose eczema. He had a generalized dermatitis but was otherwise essentially well. The rash improved with local treatment but after two weeks the patient complained of anorexia and a burning substernal pain. Shortly thereafter he was found to have albuminuria and occult blood in his feces. Two days after the dermatitis healed he developed a profuse purpura on his arms, legs, and thighs. His platelet count was normal, but he had a blood urea of 140 and a lowered serum albumin. The patient became increasingly edematous and continued to show gross albuminuria and an elevated blood pressure. ECG records show an RS pattern in leads V_{3-7} which persisted until the patient's death. Transient T-wave changes suggested localized myocardial damage. At post mortem, the kidneys showed no petechial lesions but they were edematous. Histologically, the kidney showed glomerulonephritis in a subacute phase. The heart was essentially normal. No histological abnormalities were found in the heart, but the purpura had been absent for three weeks when the patient died.

The authors suggest that the cardiac manifestations in these patients were caused by direct involvement of the heart by the purpuric process. They strongly urge that ECG studies be made on all patients having this type of syndrome, since steroid therapy might help to prevent the serious complications which can occur in this type of hypersensitivity reaction. R. W.

Deaths Associated With Steroid-Hormone Therapy. An Analysis of 18 Cases. Allanby, K. D.: Lancet **1**: 1104, 1957.

The author reviewed the records of over 400 patients treated with hormones and steroids under the supervision of the Department of Medicine at Guy's Hospital during the period from 1949 until January of 1956. Eighteen of these patients expired either while receiving the preparations or shortly following cessation of steroid or corticotrophin therapy. It was felt that steroid therapy was directly responsible for nine deaths, probably responsible for two more, and quite definitely not responsible in four of the patients. In three cases it was difficult to ascertain how important steroids or corticotrophin may have been in precipitating a fatal reaction. Seven of the eighteen patients died because of infection and four patients died from massive hemorrhage, usually from the gastrointestinal tract. Three patients died from gastrointestinal perforation, and one asthmatic appeared to have died from pulmonary embolism shortly after cessation of corticotrophin therapy. Only one asthmatic patient was included in the group of patients that died. One patient with an ankylosing spondylitis appeared to have expired from a

hypersensitivity to intravenous corticotrophin. This patient was a 59-year-old man with a history of ankylosing spondylitis of 25 years' duration. He had previously had a bilateral sympathectomy for thromboangiitis obliterans and on admission had complete rigidity of his spine, neck, and chest. A few indeterminant râles were heard at the left lung base. He was started on daily therapy with 25 units of ACTH in glucose by intravenous drip and after two days showed remarkable improvement in his joint condition. During the infusion he complained of dyspnea and developed a slight temperature elevation. The dyspnea became worse during the next two infusions and ronchi and râles were heard throughout the lungs. When the corticotrophin was stopped his symptoms subsided immediately. On the sixth day, the intravenous administration of corticotrophin had to be stopped because of his severe dyspnea. Despite what appeared to be marked improvement in his joint condition he was found dead 12 hours later. Autopsy disclosed slight right ventricular enlargement, a small amount of free fluid in each pleural cavity, and a considerable amount of thick tenacious sputum in the trachea and bronchi. There was no evidence of infection or pulmonary edema. The pelvic colon contained a small adenocarcinoma without metastases, and there was a hemorrhagic pheochromocytoma of the left adrenal gland. The author stresses the importance of avoiding the use of steroid or corticotrophin therapy in patients with tuberculosis or other chronic infections as well as in persons with a history of peptic ulcer. He also further emphasizes the importance of increasing the dose of corticotrophin or steroids during periods of stress, especially before and immediately following surgical procedures.

R. W.

The In Vitro Action of Hydrocortisone on Leucocyte Migration. Ketchel, M. M., Favour, C. B., and Sturgis, S. H.: J. Exper. Med. **107**: 211, 1958.

Heparinized venous blood was separated into cells and plasma by centrifugation. The cellular portion was washed in Hanks's solution and added to plasma. Then Hanks's solution containing appropriate concentrations of steroids being studied was added to aliquots of the same cell suspension. The cell-plasma mixture was placed in capillary tubes which were centrifuged so that a buffy coat lay between packed red cells and plasma. The tubes were incubated in a vertical position overnight. Migration of the leucocytes was then observed. Leucocyte migration was not influenced by tetrahydrocortisone (which has no known physiologic activity) or by desoxycorticosterone. Hydrocortisone decreased leucocyte migration in proportion to the concentration used and in the range in which this hormone is normally present in human blood.

E. K.

General Pharmacological Properties of 21-Hydroxy-Pregnanedione Sodium Succinate, an Intravenous Anesthetic Agent. Das, P. K., and Arora, R. B.: J. Pharmacol. & Exper. Therap. **121**: 194, 1957.

The compound 21-hydroxy-pregnanedione sodium succinate (Viadril) is a steroid which, when administered intravenously, has anesthetic activity dissociated "from one or all hormone actions." Pharmacologic data are presented on the activity of this compound in animals and a detailed comparison with thiopental sodium is made. Viadril is less depressant to respiration than thiopental sodium at anesthetic doses. In addition, Viadril shows pronouncedly relaxant and antispasmodic effects on ileal and tracheal smooth muscle. Viadril, when added to a preparation of tracheal smooth muscle in vitro, reduces the tone of the muscle and antagonizes the spasm produced by

acetylcholine or potassium chloride. Viadril is less depressant to the cardiovascular system of cats and dogs than thiopental and produces insignificant effects on heart rate, rhythm, and electrocardiogram. E. K.

Bacteriology of the Lower Respiratory Tract in Health and Chronic Diseases. Pecora, D. V., and Yegian, D.: New England J. Med. **258**: 71, 1958.

Bacterial cultures were obtained from sputum, bronchoscopic secretions, and lung tissue of a series of adequately studied patients with various disorders of the respiratory tract. The organisms most commonly encountered were streptococci, staphlococci, and *Neisseria*. The yield of these pyogenic bacteria was found to be greatest in the sputum, less in the bronchoscopic secretions, and still less from direct bronchial cultures at thoracotomy. Bacteria were found in the lung tisue itself only in cases of pulmonary abscess. Chronic infection of the lower repiratory tract with organisms other than mycobacteria or fungi are very uncommon, except in those patients with pulmonary abscess or bronchiectasis. It is suspected that what is commonly referred to as chronic bronchitis may actually be due to nonspecific irritants such as smoke or industrial fumes. H. STRYKER.

Effects of Cortisone on Trichinella Spiralis Infections in Non-Immunized Mice. Coker, C. M.: J. Parasitol. **41**: 498, 1955.

It is a well-known fact that mice develop an acquired immunity to *T. spiralis* at specified time intervals following an infection. The administration of cortisone to mice 2 days before infestation with *Trichinella* and during the period of observation significantly increased the numbers of adult worms persisting from the infestation, shifted the site of worms remaining in the intestine from the large to the small intestine, and increased the larvae counts significantly above those found in controls. Animals treated with cortisone for 2 days prior to and only 14 days after infestation responded in the same manner as the animals treated continuously until necropsy. This is considered additional evidence that an immune antibody mechanism plays a role in protecting the host from round worm infestation. The implications of these findings with reference to the treatment of human beings with cortisone for trichiniasis are discussed. E. K.